IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Rubin et al.	Group Art Unit: 1652
Serial No. Not yet assigned	Examiner: Slobodyansky, E.
Filed: Herewith	Attorney Docket No. B97-081-7
For: *KUZ, a Novel Family of Metalloproteases*	Date: May 31, 2001

This application is a divsional of USSN 09/709,126, filed Nov. 8, 2000, which is a divisional of USSN 09/285,502, filed Apr. 2, 1999, now Pat No 6,190,876, which is a divisional of USSN 08,937,931, filed Aug. 27, 1997, now Pat No 5,935,792 which is a continuing appln. of 60/053,476, filed Jul. 23, 1997 and 60/019,390, filed Aug. 29, 1996.

PRELIMINARY AMENDMENT

The Commissioner for Patents
Washington, DC 20231

Dear Commissioner:

Prior to examination of this application, please enter the following amendments:

IN THE SPECIFICATION

Please replace the paragraph beginning on line 6 of p.1 with the following:

This application is a divisional of USSN 09/709,126, filed Nov. 8, 2000, which is a divisional of USSN 09/285,502, filed April 2, 1999, now US Pat No. 6,190,876, which is a divisional of USSN 08/937,931, filed August 27, 1997, now US Pat No. 5,935,792, which claims the benefit of 60/053,476, filed Jul. 23, 1997 and 60/019,390, filed Aug. 29, 1996, each of which is incorporated by reference herein in its entirety.

Please replace the first paragraph following "BRIEF DESCRIPTION OF THE DRAWINGS" on p.3 with the following paragraph:

Figure 1 (A). Sequence alignment of predicted KUZ proteins from Drosophila (DKUZ, SEQ ID NO:2), mouse (MKUZ, SEQ ID NO:8) and Xenopus (XKUZ, SEQ ID NO:10). The full length amino acid sequence of MKUZ was deduced from the nucleotide sequence of two overlapping cDNA clones. Partial amino acid sequence of XKUZ was deduced from the nucleotide sequence of a PCR product that includes parts of the disintegrin and Cys-rich domains. The alignments were produced using Geneworks software (IntelliGenetics). Residues identical among two species are highlighted. Predicted functional domains are indicated. Amino acid sequences from which degenerate PCR primers were designed are indicated with arrows. Orthologs of *kuz* are also present in C. elegans (GenBank accession nos. D68061 and M79534), rat (Z48444), bovine (Z21961) and human (Z48579).

At p.5, line 14, before the paragraph beginning "The subject domains...", please insert the following paragraph:

Ordinarily, the allelic variants, the conservative substitution variants and the members of the *kuz* family of proteins, will have an amino acid sequence having at least 75% amino acid sequence identity with one or more of the disclosed human full length, human secreted form, mouse and *Drosophila kuz* protein sequences, more preferably at least 80%, even more preferably at least 90%, and most preferably at least 95%. Identity or homology with respect to such sequences is defined herein as percentage of amino acid residues in the candidate sequence that are identical with the known peptides, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent homology, and not considering any conservative substitutions as part of the sequence identity. N-terminal, C-terminal or internal extensions, deletions, or insertions into the peptide sequence shall not be construed as affecting homology.

Please replace the paragraph bridging p.26 and 27 with the following paragraph:

Xenopus *kuz* was cloned by PCR using degenerate primers (XK1) and (XK4) which correspond to Drosophila KUZ sequence HNFGSPHD (SEQ ID NO:2, residues 609-616) and GYCDVF (SEQ ID NO:2, residues 870-875), respectively. First strand cDNA from stage 18

Xenopus embryos was used as template in a standard PCR reaction with an annealing temperature of 50°C. A PCR product of expected size was purified and used as template for another PCR reaction using a nested primer (XK3), corresponding to Drosophila KUZ sequence EECDCG (SEQ ID NO:2, residues 688-693), and XK4. The PCR product was subcloned into Bluescript and sequenced. Anti-sense RNA was used as a probe for whole mount *in situ* hybridization of Xenopus embryos according to standard procedures (Harland, R. (1991). Meth. Cell Biol. *36*, 685-695).

At page 41, line 42, please insert the following text:

(2) INFORMATION FOR SEQ ID NO:9:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 486 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: cDNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

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TACAGCGACC AATGTAAGGA TGAATGTTGC TATGATGCCA ATCAGCCAGA AAACCTAAAG      60
TGCACATTAA AGCCTGGAAA ACAGTGCAGT CCCAGCCAGG GCCCTTGTTG CACCACTGGA     120
TGTACCTTCA AGCGAGCAGG TGAGAACTGT CGGGAGGAAT CTGACTGTGC CAAGATGGGA     180
ACTTGCAATG GCAACTCTGC TCAGTGTCCA CCATCCGAAC CAAGAGAGAA CCTGACTGAG     240
TGTAACAGGG CAACCCAAGT TTGCATCAAG GGGCAATGCT CAGGATCTAT CTGTGAGAGG     300
TATGACTTGG AAGAGTGCAC TTGCGGCAGT ACTGATGAAA AAGATGACAA AGAGCTGTGC     360
CACGTTTGCT GCATGGAGAA AATGATACCG CACACATGTG CTAGCACTGG TTCAGAAGTA     420
TGGAAAGCTT ACTTTAAAGG AAAGACTATT ACGTTACAAC CAGGATCACC TTGCAATGAA     480
TTTAAA                                                               486
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(2) INFORMATION FOR SEQ ID NO:10:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 162 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

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Tyr Ser Asp Gln Cys Lys Asp Glu Cys Cys Tyr Asp Ala Asn Gln Pro
1               5                  10                  15
Glu Asn Leu Lys Cys Thr Leu Lys Pro Gly Lys Gln Cys Ser Pro Ser
            20                  25                  30
Gln Gly Pro Cys Cys Thr Thr Gly Cys Thr Phe Lys Arg Ala Gly Glu
        35                  40                  45
Asn Cys Arg Glu Glu Ser Asp Cys Ala Lys Met Gly Thr Cys Asn Gly
    50                  55                  60
Asn Ser Ala Gln Cys Pro Pro Ser Glu Pro Arg Glu Asn Leu Thr Glu
65                  70                  75                  80
Cys Asn Arg Ala Thr Gln Val Cys Ile Lys Gly Gln Cys Ser Gly Ser
                85                  90                  95
Ile Cys Glu Arg Tyr Asp Leu Glu Glu Cys Thr Cys Gly Ser Thr Asp
            100                 105                 110
Glu Lys Asp Asp Lys Glu Leu Cys His Val Cys Cys Met Glu Lys Met
        115                 120                 125
Ile Pro His Thr Cys Ala Ser Thr Gly Ser Glu Val Trp Lys Ala Tyr
    130                 135                 140
Phe Lys Gly Lys Thr Ile Thr Leu Gln Pro Gly Ser Pro Cys Asn Glu
145                 150                 155                 160
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Phe Lys

IN THE CLAIMS

Please cancel all pending claims and enter new claims 14-33 as follows:

14. A composition comprising an antibody or antibody fragment which specifically binds a KUZ polypeptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8.

15. A composition according to claim 14, wherein the amino acid sequence is residues 320-673 of SEQ ID NO:2.

16. A composition according to claim 14 wherein the amino acid sequence is residues 212-454 of SEQ ID NO:4.

17. A composition according to claim 14, wherein the amino acid sequence is SEQ ID NO:6.

18. A composition according to claim 14, wherein the amino acid sequence is residues 213-455 of SEQ ID NO:8.

19. A composition according to claim 14, wherein the amino acid sequence is SEQ ID NO:2.

20. A composition according to claim 14, wherein the amino acid sequence is SEQ ID NO:4.

21. A composition according to claim 14, wherein the amino acid sequence is SEQ ID NO:8.

22. A composition comprising an antibody or antibody fragment which specifically binds a dominant-negative mutant of a KUZ polypeptide, said mutant consisting of (a) an amino acid sequence selected from the group consisting of SEQ ID NO:2, 4 and 6, wherein the protease domain is deleted, or (b) SEQ ID NO:2, wherein glutamate at residue 606 is substituted with alanine.

23. A composition according to claim 14, wherein the antibody or fragment thereof specifically binds the extracellular domain of the KUZ polypeptide.

24. A composition according to claim 14, wherein the antibody or fragment thereof specifically binds the intracellular domain of the KUZ polypeptide.

25. A composition according to claim 14, wherein the antibody is, or the fragment is a portion of, a polyclonal antibody.

26. A composition according to claim 14, wherein the antibody is, or the fragment is a portion of, a monoclonal antibody.

27. A composition according to claim 14, wherein the antibody is, or the fragment is a portion of, a single-chain antibody.

28. A composition according to claim 14, wherein the antibody is, or the fragment is a portion of, a mouse antibody.

29. A composition according to claim 14, wherein the antibody is, or the fragment is a portion of, a human antibody.

30. A composition according to claim 14, wherein the antibody is, or the fragment is a portion of, a mouse-human chimeric antibody.

31. A composition according to claim 14, wherein the antibody or the fragment is labeled.

32. A composition according to claim 14, wherein the antibody or the fragment is fluorescently labeled.

33. A method for making an antibody according to claim 14, comprising the step of immunizing a

cell or animal with a polypeptide comprising an amino acid sequence selected from the group consisting of residues 320-673 of SEQ ID NO:2, residues 212-454 of SEQ ID NO:4, SEQ ID NO:6, and residues 213-455 of SEQ ID NO:8 or fragment thereof sufficient to elicit said antibody, whereby the antibody is elicited.

REMARKS

The enclosed specification is identical to the specification of the prior application 09/709,126. The foregoing amendments to the enclosed specification are identical to those made in 09/709,126 except for updating the cross-reference to related applications.

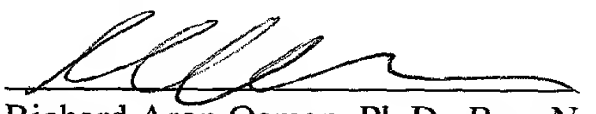
The new claims are directed to the antibody counterparts of the claims issued and allowed in 09/285,502 and 09/709,126, respectively. Claims 14-22 provide comparable limitations to those of claims 14-21 and 25 allowed in 09/709,126. Support for antibodies specific to the extracellular and intracellular domains of KUZ polypeptides is found on p.8, lines 15-17; support for polyclonal antibodies is found on p.8, lines 16-29; support for monoclonal antibodies is found on p.8, line 30 - p.9, line 16; support for single-chain antibodies is found on p.9, lines 17-19; support for KUZ-specific antibody fragments is found on p.9, lines 19-28; support for mouse antibodies is found on p.8, line 24; support for human antibodies is found on p.9, lines 7-11; support for chimeric antibodies is found on p.9, lines 11-15; support for fluorescently labeled antibodies is found on p.8, lines 7-10.

These amendments add no new matter.

The Examiner is invited to call the undersigned if she would like to amend the claims to clarify the foregoing or seeks further clarification of the claim language.

The Commissioner is hereby authorized to charge any fees or credit any overcharges relating to this communication to our Deposit Account No. 19-0750 (order no. B97-081-7).

Respectfully submitted,
SCIENCE & TECHNOLOGY LAW GROUP



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

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